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POROUS MATERIALS AND METHOD OF PRODUCTION THEREOF

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Technical Field

The present invention relates to porous materials that are soluble or dispersible in aqueous media and to methods of  
10 producing such porous materials.

Background of the Invention

15 Our co-pending international patent application PCT/GB03/03226 describes the formation of porous beads comprising a three dimensional open-cell lattice of a water-soluble polymeric material with an average bead diameter in the range 0.2 to 5mm.

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These are typically 'templated' materials formed by the removal of a non-aqueous dispersed phase from a high internal phase emulsion. The beads are freeze-dried to remove the bulk of the aqueous phase. This leaves a  
25 'skeletal' form of the emulsion behind. The beads dissolve rapidly in water and have the remarkable property that a water insoluble component dispersed in the emulsion prior to drying can also be dispersed in water on solution of the beads. Surfactant is typically present as an emulsifier.

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There are many instances in personal care products such as deodorants, skin and hair cleaning or care products or in household products such as laundry cleaning and care products or household cleaning or care products for hard and soft surfaces where it is desirable to administer hydrophobic materials in an aqueous environment. Because of the hydrophobic nature of these materials they are often reluctant to disperse in an aqueous environment. A non-limiting example of such a material is Triclosan™ (also known as Irgasan™), a chlorinated di-phenyl ether compound (5-Chloro-2-(2,4-dichlorophenoxy)phenol). This is a widely used antibacterial compound but is only sparingly soluble in water at neutral pH. It would be advantageous to have a means of rapidly forming a solution of Triclosan without the use of special solvents or alkaline pH.

The present invention is concerned with the production of bodies which are not beads and which have lower levels of surfactant present.

#### Brief Description of the Invention

In accordance with a first aspect of the invention, there is provided a porous body which is soluble or dispersible in aqueous media comprising a three dimensional open-cell lattice containing:

- (a) 10 to 95% by weight of a polymeric material which is soluble in water, and,

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- (b) less than 5% by weight of a surfactant, said porous bodies having an intrusion volume as measured by mercury porosimetry (as hereinafter described) of at least about 3 ml/g, and, with the proviso that said porous bodies are not spherical beads having an average bead diameter of 0.2 to 5mm.

The present invention also provides a method for the preparation of said porous bodies which comprises the steps of:

(I) cooling an emulsion of:

- a) An aqueous phase
- b) A water-immiscible second phase,
- c) A polymer soluble in the aqueous phase

to a temperature at which the continuous phase becomes solid, and

(II) subsequently removing the bulk of the continuous and dispersed phases of the emulsion.

The cooled emulsion retains its structure when the bulk of the phases are removed leaving a solid, polymer-containing lattice. The lattice so produced is characterised by a large surface area, which greatly assists the solution of its components.

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### Detailed Description of the Invention

In order that the present invention may be better understood and carried forth into practice, it is described below with reference to various preferred features and particular embodiments.

#### **Water soluble polymer:**

The polymeric material is a material that would be considered as "water soluble" by those skilled in the art i.e. if it forms a homogeneous solution in water. Water soluble polymers generally possess pendant polar or ionizable groups (e.g.  $-C=O$ ,  $-OH$ ,  $-N(R_1)(R_2)$  in which  $R_1$  and  $R_2$ , which may be the same or different, are independently H or (C1 to C4)alkyl,  $-N(R_3)(R_4)(R_5)^+$  in which  $R_3$ ,  $R_4$  and  $R_5$  which may be the same or different, are independently H or (C1 to C4)alkyl,  $-CON(R_6)(R_7)$  in which  $R_6$  and  $R_7$ , which may be the same or different, are H or (C1 to C4) alkyl,  $-CH_2CH_2O-$ ,  $-CO_2H$  or salts thereof,  $-SO_3H$  or salts thereof groups) on a backbone chain which may be hydrophobic.

Examples of water soluble polymeric materials include:-

- natural polymers (for example naturally occurring gums such as guar gum or locust bean gum or a polysaccharide such as dextran or cellulose;
- cellulose derivatives for example xanthan gum, xyloglucan, cellulose acetate, methylcellulose, methylethylcellulose, hydroxyethylcellulose, hydroxyethylmethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose

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(HPMC), hydroxypropylbutylcellulose,  
ethylhydroxyethylcellulose, carboxymethylcellulose and its  
salts (eg the sodium salt - SCMC), or  
carboxymethylhydroxyethylcellulose and its salts (for  
5 example the sodium salt);

- homopolymers of any one of the monomers listed in Table 1  
below;

- 10 • copolymers prepared from two or more monomers listed in  
Table 1 below;

and mixtures thereof

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Table 1

	vinyl alcohol,
	acrylic acid,
5	methacrylic acid
	acrylamide,
	methacrylamide
	acrylamide methylpropane sulphonates
	aminoalkylacrylates
10	aminoalkylmethacrylates
	hydroxyethylacrylate
	hydroxyethylmethacrylate
	vinyl pyrrolidone
	vinyl imidazole
15	vinyl amines
	vinyl pyridine
	ethyleneglycol
	ethylene oxide
	ethyleneimine
20	styrenesulphonates
	ethyleneglycolacrylates
	ethyleneglycol methacrylate

25 When the polymeric material is a copolymer it may be a statistical copolymer (heretofore also known as a random copolymer), a block copolymer, a graft copolymer or a hyperbranched copolymer.

30 Comonomers other than those listed in Table 1 may also be included in addition to those listed if their presence does

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not destroy the water soluble or water dispersible nature of the resulting polymeric material.

Examples of suitable homopolymers include polyvinylalcohol,  
5 polyacrylic acid, polymethacrylic acid, polyacrylamides  
(such as poly-N-isopropylacrylamide), polymethacrylamide;  
polyacrylamines, polymethylacrylamines, (such as  
polydimethylamino-ethyl-methacrylate and poly-N-morpholino-  
ethylmethacrylate, polyvinyl-pyrrolidone,  
10 polyvinylimidazole, polyvinylpyridine, polyethylene-imine  
and ethoxylated derivatives thereof.

**Product Form:**

15 The bulk density of the porous polymeric bodies is  
preferably in the range of from about 0.01 to about 0.2  
g/cm<sup>3</sup>, more preferably from about 0.02 to about 0.09 g/cm<sup>3</sup>,  
and most preferably from about 0.03 to about 0.08 g/cm<sup>3</sup>.

20 The intrusion volume of the porous bodies as measured by  
mercury porosimetry (as hereinafter described) is at least  
about 3 ml/g, more preferably at least about 4 ml/g, even  
more preferably at least about 5ml/g, and most preferably at  
least about 6 ml/g. For example, the intrusion volume may  
25 be from about 3 ml/g to about 30 ml/g, preferably from about  
4 ml/g to about 25ml/g, more preferably from about 10 ml/g  
to about 20ml/g.

Intrusion volume provides a very good measure (in materials  
30 of this general type) of the total pore volume within the  
porous bodies of the present invention.

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The porous bodies may be in the form of powders, beads (but not spherical beads having an average bead diameter of 0.2 to 5 mm) or moulded bodies. Powders may be prepared by the disintegration of porous bodies in the form of beads or  
5 disintegration of bodies during other stages of the production process.

Preferred forms are:

- 10 • powders of a number average diameter of less than 0.2mm, more preferably in the range 1-150 microns,
- non-spherical particles in the size range 0.2-5mm, and,
- 15 • particles and bodies larger than 5mm.

**Porous bodies as carriers:**

The porous bodies of the present invention have utility as a  
20 means of forming a solution of the polymer, but optionally include within the lattice hydrophobic materials to be dispersed when the polymeric bodies are dispersed in an aqueous medium. Dispersion into an aqueous medium of such hydrophobic materials is much improved.

25 The hydrophobic materials may be incorporated into the lattice by dissolving them in the discontinuous oil phase of an oil-in-water emulsion from which the lattice is made.

30 The present invention also includes, in a further aspect, solutions or dispersions comprising water soluble polymer



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and a hydrophobic material obtainable by exposing to an aqueous medium porous bodies according to the present invention, wherein said bodies comprise the hydrophobic material.

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The use of the porous bodies of the present invention facilitates this dispersion and in many cases enables hydrophobic materials to be dispersed more effectively than previously. This can greatly improve the activity of the hydrophobic materials. For  
10 example, in the case of Triclosan, a dispersion of particles can be made in water but a large part of the Triclosan remains undissolved and therefore unavailable.

It may be required to disperse the hydrophobic materials at the  
15 point where the product is being used. In this case the porous bodies of the present invention will be contained in the product until it is used by exposing it to an aqueous environment, at which time the water-soluble/dispersible lattice of the porous body will break down releasing the hydrophobic material.

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The porous bodies of the present invention may be used to introduce hydrophobic materials into products, for example, liquid products during the manufacture of the products. In this case the lattice of the porous bodies of the present  
25 invention will break down when the porous bodies contact an aqueous environment during manufacture releasing the hydrophobic material in a form in which it can be more readily incorporated into the product being manufactured.

30 The porous bodies of the present invention may be used to transport materials to sites where they can be incorporated

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into products. By converting liquid products into porous bodies the need to transport large amounts of liquids can be avoided resulting in significant cost savings and safer transport of materials which are potentially hazardous when transported in a liquid form. Materials which would be potentially unstable if stored or transported in liquid form may be incorporated into the porous bodies of the present invention and stored or transported with less risk of degradation.

The incorporation of potentially unstable hydrophobic materials, for example vaccines, vitamins or perfumes, into the porous bodies of the present invention may protect them from degradation during storage prior to use.

Some specific examples of products in which the porous bodies of the present invention may be used are given below. These are given as examples only and are not intended to limit the applicability of the present invention. Those skilled in the art will however realise that the porous bodies of the present invention will have utility in other areas not specifically exemplified herein.

Hydrophobic materials that are released from the porous bodies of the present invention at the time of use may include:-

- antimicrobial agents, for example: triclosan, climbazole, octapyrox, ketoconazole, phthalimoperoxyhexanoic acid (PAP), quaternary ammonium compounds, colloidal silver, zinc oxide.

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- antidandruff agent for example: zinc pyrithione
- skin lightening agents for example 4-ethylresorcinol
- 5 • fluorescing agents for example: 2,5-bis(2-benzoxazolyl) thiophene for use on fabrics (such as cotton, nylon, polycotton or polyester) in laundry products
- skin conditioning agents, for example cholesterol
- 10 • antifoaming agents for example isoparaffin
- hair conditioning agents for example quaternary ammonium compounds, protein hydrolysates, peptides, ceramides and
- 15 hydrophobic conditioning oils for example hydrocarbon oils such as paraffin oils and/or mineral oils, fatty esters such as mono-, di-, and triglycerides, silicone oils such as polydimethylsiloxanes (e.g. dimethicone) and mixtures thereof
- 20 • fabric conditioning agents for example quaternary ammonium compounds having 1 to 3, preferably 2 optionally substituted (C8-C24) alk(en)yl chains attached to the nitrogen atom by one or more ester groups; hydrophobic
- 25 mononparticles such as a sucrose polyester for example sucrose tetra-tallowate; silicones for example polydimethylsiloxane
- thickening agents for example hydrophobically modified
- 30 cellulose ethers such as modified hydroxyethylcelluloses

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- dyes for example dyes intended to change the colour of fabrics, fibres, skin or hair.
- UV protecting agents such as sunscreens for example octyl methoxycinnamate (Parsol MCX), butyl methoxydibenzoylmethane (Parsol 1789) and benzophenone-3 (Uvinul M-40), ferulic acid.
- bleach or bleach precursors for example 6-N-phthalimidoperoxyhexanoic acid (PAP) or photobleaching compounds. Dispersing the bleach from the porous bodies of the present invention results in the bleach being more finely dispersed and reduces the spot damage seen when larger particles of the bleach contact a fabric
- antioxidants for example hydrophobic vitamins such as vitamin E, retinol, antioxidants based on hydroxytoluene such as Irganox or commercially available antioxidants such as the Trollox series.
- insecticides, pesticides, herbicides that are stored as solid compositions before use but which are made up into liquid for spraying onto animals or crops
- perfumes or flavourings or precursors thereto
- pharmaceutically or veterinary active materials. There is a need for pharmaceutical compositions which can be taken by the consumer without the need to ingest the composition with a drink such as water. These compositions interact

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with the moisture in the oral cavity to release the active ingredient which is then ingested by the consumer. By incorporating the pharmaceutically or veterinary active molecule in the porous bodies of the present invention, pharmaceutical compositions which meet this need can be prepared.

- In a similar way to that described above pharmaceutical and veterinary active ingredients may be formulated so that they release the active material into the nasal, ocular, pulmonary or rectal cavities or on the skin where they may act topically or they may be absorbed transdermally to act systemically
- By using the appropriate polymeric material in the lattice of the porous bodies of the present invention, porous bodies can be made that remain intact until the conditions (for example temperature or pH) change to those under which dispersion can occur. Thus dispersion can be delayed until a certain temperature has been reached or until the pH has changed to a suitable value such as would occur as the porous bodies pass down the GI tract. The acidity in the GI tract reduces down the GI tract and porous bodies which disperse hydrophobic actives only when the porous bodies are exposed to higher pH conditions enable pharmaceutically or veterinary active materials to be released only in the intestine having passed through the stomach intact.

Examples of situations where the porous bodies of the present invention are used to incorporate a hydrophobic

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material into a product during the manufacture of that product include:-

- the introduction of hydrophobic materials such as  
5 fluorescers; enzymes; bleaches; hydrophobic polymers for  
example hydrophobically modified polyacrylates, silicones,  
hydrophobically modified polyvinylpyrrolidone, sulpho  
alkyl polysaccharides, Jaguar and JR polymers; fatty  
alcohols or acids; dyes for example shading dyes or black  
10 dyes for colour recovery into laundry products.
- the use of porous bodies according to the present  
invention containing hydrophobic dyes in the manufacture  
of water soluble inkjet compositions.
- 15 • the introduction of porous bodies containing different  
hydrophobic materials enables a manufacturer to produce a  
single base formulation into which the desired hydrophobic  
materials may be introduced by the use of the appropriate  
20 porous body of the present invention.
- the use of porous bodies containing hydrophobic polymers  
which disperse into water as the lattice breaks down to  
form a latex. The use of such latexes containing  
25 appropriate hydrophobic polymers deposited onto fabric  
imparts crease resistance or easy-iron properties to the  
fabric.

The porous bodies of the present invention may include within the  
30 lattice, water soluble materials which will be dispersed when the

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polymeric bodies are dispersed in an aqueous medium. The water soluble materials may be incorporated into the lattice by dissolving them in the liquid medium from which they are made.

5 Examples of suitable water soluble materials include:-

- Water soluble vitamins such as vitamin C;
- water soluble fluorescers such as the 4,4'-bis(sulfo-  
10 styryl)biphenyl disodium salt (sold under the trade name Tinopal CBS-X;
- activated aluminium chlorohydrate;
- 15 • transition metal complexes used as bleaching catalysts;
- water soluble polymers such as polyesters isophthalic acid), gerol, xanthan gum, or polyacrylates;  
diethylenetriaminepentaacetic acid (DTPA);  
20 or mixtures thereof

The porous bodies of the present invention may include within the lattice, materials which will be dispersed as  
25 very small particles when the polymeric bodies are dispersed in an aqueous medium. These materials may be incorporated into the lattice by dissolving or dispersing them in the liquid medium from which the porous bodies are made. If the particles are less than 1 micron, preferably less than 0.5  
30 micron and they are incorporated into skincare products then

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the particles will not be felt by the user as the dispersed porous bodies are applied to the skin.

**Surfactant:**

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Surfactant is present at a level of less than 5%wt in the porous bodies. The surfactant may be non-ionic, anionic, cationic, or zwitterionic.

10 Examples of suitable non-ionic surfactants include ethoxylated triglycerides; fatty alcohol ethoxylates; alkylphenol ethoxylates; fatty acid ethoxylates; fatty amide ethoxylates; fatty amine ethoxylates; sorbitan alkanoates; ethylated sorbitan alkanoates; alkyl ethoxylates;  
15 pluronics™; alkyl polyglucosides; stearyl ethoxylates; alkyl polyglycosides.

Examples of suitable anionic surfactants include alkylether sulfates; alkylether carboxylates; alkylbenzene sulfonates;  
20 alkylether phosphates; dialkyl sulfosuccinates; alkyl sulfonates; soaps; alkyl sulfates; alkyl carboxylates; alkyl phosphates; paraffin sulfonates; secondary n-alkane sulfonates; alpha-olefin sulfonates; isethionate sulfonates.

25 Examples of suitable cationic surfactants include fatty amine salts; fatty diamine salts; quaternary ammonium compounds; phosphonium surfactants; sulfonium surfactants; sulfonxonium surfactants.

30 Examples of suitable zwitterionic surfactants include N-alkyl derivatives of amino acids (such as glycine, betaine,



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aminopropionic acid); imidazoline surfactants; amine oxides; amidobetaines.

Mixtures of surfactants may be used, however it is preferred  
5 that only low levels of surfactant (preferably less than 3%wt, more preferably less than 1%wt) or none at all are present.

**Method of Preparation:**

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As noted above, one method suitable for preparing the porous bodies comprises the steps of: cooling a polymer-containing oil-and-water emulsion to a temperature at which the continuous phase becomes solid, and subsequently removing  
15 the bulk of the continuous and dispersed phases.

Accordingly a further aspect of the present invention, there is provided a method the preparation of water dispersible or water soluble porous bodies comprising a three dimensional  
20 open-cell lattice containing: 10 to 95% by weight of a polymeric material which is soluble in water and less than 5% by weight of a surfactant, said porous bodies having an intrusion volume as measured by mercury porosimetry (as herein described) of at least about 3 ml/g with the proviso  
25 that said porous body is not a spherical bead having an average bead diameter of 0.2 to 5mm comprising the steps of:

a) providing an intimate mixture of the polymer in a liquid  
30 medium

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- b) providing a fluid freezing medium at a temperature effective for rapidly freezing the liquid medium;
- c) cooling the liquid medium with the fluid freezing medium at a temperature below the freezing point of the liquid medium for a period effective to rapidly freeze the liquid medium; and
- (d) freeze-drying the frozen liquid medium to form the bodies by removal of the liquid medium by sublimation.

The intimate mixture of the surfactant in the liquid medium is preferably an oil-in-water emulsion comprising a continuous aqueous phase containing the polymeric material and a discontinuous oil phase.

When the porous body is to be in the form of a powder the cooling of the liquid medium may be accomplished by spraying the liquid medium, preferably in an atomised form, into the fluid freezing medium.

Porous bodies in the form of moulded bodies may be made by pouring the liquid medium into a mould and cooling the liquid medium by the fluid freezing medium. In a preferred process of the invention to make moulded bodies, the liquid medium is poured into a pre-cooled mould surrounded by fluid freezing medium.

The frozen liquid medium may be freeze-dried by exposing the frozen liquid medium to high vacuum. The conditions to be used will be well known to those skilled in the art and the

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vacuum to be applied and the time taken should be such that all the frozen liquid medium present has been removed by sublimation.

- 5 In the case of moulded porous polymeric bodies freeze-drying may take place with the frozen liquid medium still in the mould. Alternatively, the frozen liquid medium may be removed from the mould and subsequently freeze-dried.
- 10 The freeze-drying step may be performed for up to around 72 hours in order to obtain the porous bodies of the present invention.

The above process preferably uses an oil-in-water emulsion comprising a continuous aqueous phase and a discontinuous oil phase.

Where present the surfactant can act as an emulsifier. Surfactants suitable for use as emulsifiers in oil-in-water emulsions preferably have an HLB value in the range 8 to 18.

The discontinuous oil phase of the oil-in-water emulsion comprises a material which is immiscible with the continuous phase, which preferably freezes at a temperature above the temperature which is effective for rapidly freezing the aqueous medium and which is removable by sublimation during the freeze drying stage.

The discontinuous oil phase of the emulsion may be selected from one or more from the following group of organic solvents:

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- alkanes, such as heptane, n-hexane, isooctane, dodecane, decane;
- cyclic hydrocarbons, such as toluene, xylene, cyclohexane;
- halogenated alkanes, such as dichloro-methane, dichloro-ethane, trichloro-methane (chloroform), fluoro-trichloro-methane and tetrachloro-ethane;

10 • esters such as ethyl acetate;

• ketones such as 2-butanone;

• ethers such as diethyl ether;

15

• volatile cyclic silicones such as cyclomethicone;

and mixtures thereof

20 Preferably, the organic solvent comprises from about 10 % to about 95 % v/v of the emulsion, more preferably from about 20 % to about 60 % v/v. A preferred solvent is cyclohexane as the freezing point of cyclohexane is higher than that of water and the specific heat capacity for cyclohexane is much lower than  
25 that of water. This induces rapid freezing of the emulsion.

Preferably, the fluid medium is at a temperature below the freezing point of all of the components and is preferably at a much lower temperature to facilitate rapid freezing. The  
30 fluid freezing medium is preferably a liquified substance

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which is a gas or vapour at standard temperature and pressure. The liquified fluid freezing medium may be at its boiling point during the freezing of the liquid medium or it may be cooled to below its boiling point by external cooling means. The fluid freezing medium may be selected from one or more of the following group; liquid air, liquid nitrogen (b.p.  $-196^{\circ}\text{C}$ ), liquid ammonia (b.p.  $-33^{\circ}\text{C}$ ), liquified noble gas such as argon, liquefied halogenated hydrocarbon such as trichloroethylene, chlorofluorocarbons such as Freon (RTM), hexane, dimethylbutene, isooheptane or cumene. Mixtures of organic liquids and solid carbon dioxide may also be used as the fluid freezing medium. Examples of suitable mixtures include chloroform or acetone and solid carbon dioxide ( $-77^{\circ}\text{C}$  and diethyl ether and solid carbon dioxide ( $-100^{\circ}\text{C}$ ).

The fluid medium is removed during freeze drying, preferably under vacuum and is preferably captured for reuse. Due to the very low boiling temperature, inertness, ease of expulsion and economy, liquid nitrogen is the preferred fluid freezing medium.

The emulsions are typically prepared under conditions which are well known to those skilled in the art, for example, by using a magnetic stirring bar, a homogenizer, or a rotator mechanical stirrer.

The porous polymeric bodies produced usually comprise of two types of pores. One is from the sublimation of solid ice. The other kind of pore structure results from the sublimation of the oil phase.

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The method for producing porous bodies according to the present invention, will now be more particularly described, by way of example only, with reference to the accompanying Examples.

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### Examples

10 Example 1 - Hydrophilic Polymer (PVA) used with hydrophobic active (Triclosan).

15 An emulsion was prepared as follows: Polyvinylalcohol (0.89 g, MW 9,000-10,000) was dissolved in water (12 ml) to form the continuous phase. To this aqueous solution was added the dispersed phase comprising triclosan (0.1 g) in cyclohexane (12 ml) with vigorous stirring (using a type RW11 Basic IKA paddle stirrer).

20 The emulsion was sprayed into liquid nitrogen using a trigger spray and the resulting frozen powder was freeze-dried to form a powder. The freeze-drier, an Edwards Supermodulyo, used an average vacuum of 0.2mbar and operated at -50 °C.

25 This powder dissolved readily into water to form a clear 'solution' of Triclosan.